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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 09/049,227 | 03/27/98 | REDMON M | 4821-304 |

HM22/0923

PENNIE & EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK NY 10036-2711

| EXAMINER | |
|---|---|
| DELACROIX MUIRHEI,C | |
| **ART UNIT** | **PAPER NUMBER** |
| 1654 | 10 |

**DATE MAILED:** 09/23/99

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

## Office Action Summary

| Application No. | Appli(s) |
|---|---|
| 09/049,227 | Redmon et al |
| **Examiner** | **Group Art Unit** |
| C. Delacroix-M | 1654 |

☒ Responsive to communication(s) filed on 7/22/99.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) 1-38 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-38 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*— SEE OFFICE ACTION ON THE FOLLOWING PAGES —*

## DETAILED ACTION

1. Claims 13, 14, 16-18, 21-25, 28-30, 35, 36-38 are rejected under 35 U.S.C. 102(b) as being anticipated by EPA 0693281 ('281).

2. Claims 1-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over EPA '281 in view of the Physicians Desk Reference (PDR), 50th edition (1996).

3. Claims 1-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over EPA '281 in view of PDR as applied to claims 1-35 above, and further in view of Wirth et al.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Newly added claims 36-38 fall under the rejections set forth in the previous office action mailed Dec. 22, 1998 for reasons already of record. Additional comments with respect to said claims are made hereinbelow.

### *Response to Amendment*

The following is responsive to Applicant's amendment received Jun. 22, 1999.

No claims are cancelled. New claims 36-38 are added. Claims 1-38 are currently pending.

The previous objection to the disclosure (¶ 1 and 2 of the office action mailed Dec. 22, 1998) **is withdrawn** in view of Applicant's submission an abstract that is more commensurate in scope with the disclosure.

The previous objection of claims 34 and 33 under 37 CFR 1.75, (¶ 6 of the office action mailed Dec. 22, 1998)

The previous rejections under 35 USC 112, paragraph 2, (¶ 3-5 of the office action mailed Dec. 22, 1998), **are withdrawn** in view of Applicant's amendment and the remarks contained therein.

Applicant's arguments traversing (1) the previous claims rejection under 35 USC 102(b) over EPA 693281 ('281); (2) the previous claims rejection under 35 USC 103(a) over EPA '281 in view of PDR, 50th edition ; and (3) the previous claims rejection under 35 USC 103(a) over EPA

and PDR and further in view of Wirth et al. (¶ 7-12 of the office action mailed Dec. 22, 1998), have been considered but are not found to be persuasive.

Said rejections are maintained essentially for the reasons given previously in the office action mailed Dec. 22, 1998, with the following additional comment:

***Claims rejection under 35 USC 102(b)***:

Concerning the previous rejections of claims 13, 14, 16-18, 21-25, 28-30, 35, 36-38 under 35 USC 102(b) over EPA '281, it is Applicant's position that the claimed compositions are distinct over the prior art for the following reasons: First of all, Applicant contends that EPA '281 discloses fluoxetine compositions in tablet form that dissolve within three minutes , whereas Applicant's compressed tablet compositions require more than three minutes to dissolve and disperse uniformly in the DISSOLUTION TEST. Next, Applicant argues that EPA '281, while disclosing lactose free fluoxetine formulations, fails to appreciate the benefits of using lactose-free compositions. Applicant has discovered that lactose-free fluoxetine compositions are unexpectedly stable chemically. EPA '281, on the other hand, is silent with respect to the stability of the lactose-free compositions. Moreover, Applicant asserts that claim 21 recites "consisting essentially of" language which excludes amounts of lactose and water that would render the resulting composition unstable. Finally, Applicant argues that claims 22-25, 28-29 and 36 recite anhydrous or non-hygroscopic formulations of fluoxetine, that is to say that the claimed compositions are substantially free of water. EPA '281, on the other hand, is silent to the use of anhydrous or non-hygroscopic formulations of fluoxetine. EPA '281 discloses methods of making the disclosed formulations, wherein conventional direct compression techniques are used to avoid additional water from the atmosphere; however, there is no drying process that removes remaining unbound water. EPA '281 does not discuss the incompatibility of fluoxetine, lactose and water. Thus, the claims cannot be anticipated by EPA '281.

Said arguments have been considered but are not found to be persuasive.

It is the Examiner's position that the claims remain anticipated by EPA '281. To begin with, Applicant's argument concerning the amount of time that the claimed compositions must dissolve, i.e. more than three minutes in the DISSOLUTION TEST, is unconvincing since said argument

does not distinguish, structurally, the claimed composition over the composition of the prior art. Applicant's claims are drawn to compositions and must differ structurally or physically over compositions disclosed by the prior art. Even if said argument were to be given any weight, the claimed compositions are anticipated by the prior art. Thus, absent evidence to the contrary, it would be inherent that some of the compositions would dissolve in more than three minutes as well.

Regarding Applicant's argument that EPA '281, while disclosing lactose free fluoxetine formulations, fails to appreciate the benefits of using lactose-free compositions, the Examiner respectfully submits that said argument is irrelevant in view of the fact that the preferred compositions in EPA '281 disclose lactose-free fluoxetine compositions. It matters not that Applicants have discovered an unexpected property to the disclosed lactose-free fluoxetine compositions, i.e. chemically stable. The courts have held "the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable". *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In other words, a product disclosed by the prior art does not become patentable upon the discovery of a new or unexpected property. Please also refer to MPEP 2112.

Furthermore, the use of "consisting essentially of language", which excludes the presence of water and lactose in the claimed fluoxetine compositions is noted; however, Applicant is reminded that EPA '281 discloses compositions that do not contain lactose or water. Absent evidence to the contrary, the EPA '281 compositions are substantially free of water. This same reasoning also applies to the argument that EPA '281 is silent to the use of anhydrous or non-hygroscopic formulations of the disclosed fluoxetine compositions. Since, the disclosed compositions in EPA '281 do not set forth water as an ingredient or component, it would appear that the compositions are inherently anhydrous or non-hygroscopic . The incompatibility of fluoxetine, lactose and water is not discussed because the compositions in Examples 2-20, which anticipate Applicant's claims, do not disclose fluoxetine formulations containing lactose or water.

Finally, Applicant's argument, that EPA '281 discloses a method of preparing fluoxetine compositions wherein said method lacks a drying process, is not germane to the issue of

patentability of the claimed compositions. Applicant's claims are not drawn to processes of making the claimed compositions.

All of Applicant's arguments traversing the previous rejection have been conclusory and unsupported by facts. It is held that "conclusory statements are not probative unless supported by facts". Please see *Ex parte Gray*, 10 USPQ 2d 1922 (BPAI 1989).

It is for the reasons described hereinabove in addition to the reasons given previously in the office action mailed Dec. 22, 1998, that claims 13, 14, 16-18, 21-25, 28-30, 35 and newly added claims 36-38 stand rejected.

***Claims rejections under 35 USC 103(a):***

Applicant's arguments with respect to EPA '281, set forth hereinabove, apply to the 35 USC 103(a) rejection as well.

Concerning the secondary references to PDR 50th edition and Wirth et al., Applicant argues that in addition to being silent to lactose-free fluoxetine compositions as well as anhydrous or hygroscopic formulations, the PDR reference fails to disclose or suggest formulating one of the optically pure enantiomers of fluoxetine into a pharmaceutical composition. Instead PDR teaches that both of the fluoxetine enantiomers have essentially equivalent pharmacological activity. In view of said teaching, Applicant contends that one of ordinary skill in the art would not be motivated to formulate pharmaceutical compositions using one optically pure enantiomer. The PDR may render the use of an optically pure enantiomer "obvious to try". Finally, Applicant again asserts that the PDR reference combined with EPA '281 does not disclose the improved stability of the claimed compositions.

With respect to the Wirth reference, it is submitted that Wirth fails to cure the deficiencies of EPA '281 and PDR. Specifically, Wirth does not disclose anhydrous or non-hygroscopic fluoxetine compositions that disintegrate in more than three minutes or that pharmaceutical formulations may comprise one optically pure fluoxetine enantiomer. Moreover, Wirth relates to conventional lactose containing tablets. One of ordinary skill in the art, given the teachings of Wirth, would not be motivated to combine the lactose containing fluoxetine compositions of Wirth with the rapidly disintegrating lactose-free fluoxetine compositions of EPA '281 or the

capsules of the PDR reference. It is submitted that, the references either singly or in combination fail to disclose Applicant's claimed compositions.

Said arguments have been considered but are not found to be persuasive.

The PDR reference was relied upon for its teaching that both the R- and S- enantiomers of fluoxetine are specific and potent serotonin uptake inhibitors, thus having equivalent pharmacologic activity. In view of this teaching, the Examiner maintains that modification of EPA '281 to incorporate an optically pure enantiomer of fluoxetine would have been motivated by the reasoned expectation of producing an equally effective pharmaceutical product. The Examiner submits that PDR reasonably suggests that either one of the enantiomers would be effective in a pharmaceutical formulation. Furthermore, the courts have held that " an invention is 'obvious to try' where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful." *Merck & Co. V. Biocraft Laboratories Inc.*, 10 USPQ 2d 1843 (Fed. Cir. 1989). In this case, instead of many possible choices to choose from, PDR presents only two possible choices, each of which is disclosed by PDR as being equally successful.

Finally, regarding Applicant's arguments that the prior art, combined, does not suggest the improved stability of the claimed compositions, the Examiner again maintains that a product disclosed by the prior art does not become patentable upon the discovery of a new or unexpected property.

Next, responding to Applicant's arguments concerning the Wirth reference, the Examiner submits that the Wirth reference was relied upon for its teaching that the presence of lactose in pharmaceutical compositions containing fluoxetine causes fluoxetine to undergo the Maillard reaction producing unwanted degradation products. Please refer to the abstract. In view of said teaching, one of ordinary skill in the art would have been motivated to modify the only composition in EPA '281 that contains lactose (Example 1), by removing the lactose so as to not compromise the stability of the fluoxetine compositions.

Finally, contrary to Applicant's arguments that it would not be obvious to remove disintegrants in the claimed compositions, the Examiner maintains that the omission of a

disintegrant in the claimed compositions is obvious and well within the capability of the skilled artisan. Absent evidence to the contrary, omission of a disintegrant would result in compositions that do not rapidly disintegrate.

In addition to the reasons given previously in the office action mailed Dec. 22, 1998, it is for the reasons described hereinabove in addition to the reasons given previously in the office action mailed Dec. 22, 1998 , that claims 1-35 and newly added claims 36-38 stand rejected.

***Conclusion***

Hence, claims 1-38 stand rejected.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is (703) 306-3227. The examiner can normally be reached on Tue-Fri from 8:30 to 6:00. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward PhD, can be reached on (703) 308-4028. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

CDM

Sep. 15, 1999

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600